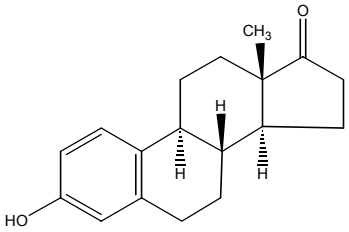
ESTROGENS (NOT CONJUGATED)

ESTRONE
CAS No. 53-16-7
First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

Estrone is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.6, 1974; IARC V.21, 1979; IARC S.4, 1982; IARC S.7, 1987). When administered orally, topically, subcutaneously, or by implantation, estrone induced an increased incidence of mammary tumors in mice. In rats, subcutaneous injection or implantation of estrone induced pituitary, adrenal, and mammary tumors, as well as bladder tumors in association with bladder stones. When administered subcutaneously, estrone caused kidney tumors in both castrated and intact male hamsters, and pituitary adenomas in castrated male hamsters.

There is inadequate evidence for the carcinogenicity of estrone in humans (IARC V.6, 1974). There is sufficient evidence for the carcinogenicity of steroidal estrogens in humans. Studies of humans given estrone alone were not available to IARC Working Groups (IARC V.6, 1974; IARC V.21, 1979; IARC S.4, 1982; IARC S.7, 1987). However, studies strongly suggest that administration of estrogens is associated with an increased incidence of endometrial carcinoma in humans, and there is no evidence that estrone is different from other estrogens in this respect. An IARC Working Group concluded that in the absence of adequate data for humans, it is reasonable to regard estrone as if it presented a carcinogenic risk to humans (IARC V.21, 1979).

PROPERTIES

Estrone is an odorless white crystalline solid. It is insoluble in water; slightly soluble in absolute ethanol, ether, and vegetable oils; and soluble in acetone, fixed oils, dioxane, pyridine, fixed alkaline hydroxide solutions, and chloroform. Estrone is available in the United States as a grade containing 97%-103% active ingredient. When heated to decomposition, it emits acrid smoke and fumes.

USE

Estrone is a metabolite of the most potent naturally occurring estrogen, estradiol-17β (IARC V.21, 1979). It is secreted by the ovaries in normal adult cycling females and by the placenta in pregnant females. It is essential for the growth and normal maintenance of the uterine lining, for the development of the accessory and secondary female sex characters, and for support of pregnancy (Prosser, 1973). Estrone, in its various forms, is used in human medicine to treat conditions such as amenorrhea, breast carcinoma, hypogenitalism, menopausal syndrome, postmenopausal osteoporosis, postpartum breast engorgement, prostatic carcinoma, and senile vaginitis. In such applications, it is frequently combined with other hormones or medicinals such as barbiturates and tranquilizers (IARC V.6, 1974). Additionally, estrone has been used in hormonal skin preparations for cosmetic use at levels of < 0.1% (IARC V.21, 1979). Therapeutically, it can serve as an oral contraceptive in combination with progestins, prevent threatened or habitual abortion, and treat dwarfism and acne at the early pubescent stage (HSDB, 1998).

PRODUCTION

Current production and import and export volumes were not available. Chemcyclopedia 98 lists two U.S. suppliers of estrone, and the 1998 Chemical Buyers Directory names three suppliers of estrone and salts or esters (Rodnan, 1997; Tilton, 1997). Currently, the USITC does not identify manufacturers for individual estrogens (USITC, 1988-1991, 1993-1995). It did identify one company that produced an unspecified amount of estrone from 1983 through 1985 (USITC, 1984-1986). The 1984 Chem Sources USA directory listed two other companies as manufacturers (Chem Sources, 1984). In 1983, U.S. imports of estrone totaled 55 lb (USITCa, 1984). The 1979 TSCA Inventory reported that a single company imported 500 lb of estrone in 1977 (TSCA, 1979). Commercial production of estrone in the United States was first reported in 1941 by the U.S. Tariff Commission (IARC V.21, 1979).

EXPOSURE

The primary routes of potential exogenous human exposure to estrone are injection of pharmaceuticals containing the compound, dermal contact, and inhalation. Injection dosages range from 0.1 mg/week up to 5 mg/day, depending on symptoms. For treatment of atrophic vaginitis, estrone may be administered by vaginal suppository (IARC V.6, 1974; IARC V.21, 1979). Estrone has also been used in hormonal skin preparations for cosmetic use at concentrations of < 0.1%. Unspecified estrogen and estrogenic hormones, which are believed to consist mainly of estrone, have been used in hormonal skin preparations (< 0.1%-5%), moisturizing lotions (1%-5%), wrinkle-smoothing creams, hair conditioners, hair straighteners, shampoos, and grooming aid tonics (< 0.1%) (IARC V.21, 1979). Potential occupational exposure may occur through inhalation or dermal contact during the production, formulation, packaging, or administration of estrone. The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 2,770 workers were potentially exposed to estrone in the workplace in 1970 (NIOSH, 1976). The National Occupational Exposure Survey (1981-1983) estimated that 4,444 total workers, including 3,848 women, potentially were exposed to estrone (NIOSH, 1984). Estrone is found in the urine of pregnant women, mares, bulls, and stallions; in the follicular liquor of many animals; in human placentas; and in palm kernel oil. It has also been found in plant material, such as the roots of moghat and in the pollen grains of the date palm (IARC V.21, 1979).

REGULATIONS

Because this chemical is used as a pharmaceutical and in low quantities relative to other chemicals, estrone is not regulated by EPA. There may be a small pollution problem relative to hospital wastes. FDA regulates estrone under the Food, Drug, and Cosmetic Act (FD&CA) as a prescription drug approved for human use. FDA has ruled that estrogens for general use must carry patient and physician warning labels concerning use, risks, and contraindications. OSHA regulates estrone under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-60.